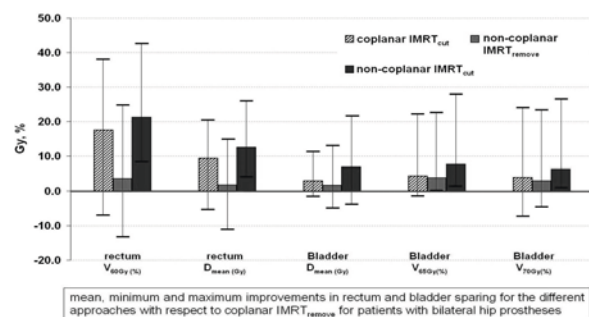


beamlets that would deliver dose to the target after passing a prosthesis (IMRT_{remove}, recommended by AAPM), and ii) exclusion of only those beamlets including a 5 mm margin (IMRT_{cut}). Plans with optimized coplanar and non-coplanar beam arrangements were generated. Differences in PTV coverage and sparing of organs at risk (OARs) were quantified. The impact of beam number on plan quality was evaluated.

Results: Especially for patients with bilateral hip prostheses, IMRT_{cut} significantly improved rectum and bladder sparing compared to IMRT_{remove}. For 9-beam coplanar plans, rectum V_{60Gy} reduced by 17.5% ± 15.0% (maximum 37.4%, $p = 0.036$) and rectum D_{mean} by 9.4% ± 7.8% (maximum 19.8%, $p = 0.036$). PTV coverage was similar, except for one patient who had a V_{95%} of only 22.3% for IMRT_{remove}, compared to 99.1% for IMRT_{cut}. Improved PTV coverage was only possible with a higher dose in all OARs (see figure). Further improvements in OAR sparing were achieved by using non-coplanar beam set-ups, reducing rectum V_{60Gy} by another 4.6% ± 4.9% ($p = 0.012$) for non-coplanar 9-beam IMRT_{cut} plans. Large reductions in rectum dose delivery were also observed when increasing the number of optimized beam directions in the plans. For bilateral implants, rectum V_{60Gy} was 37.3% ± 12.1% for coplanar 7-beam IMRT_{cut} plans which reduced on average by 13.5% (maximum 30.1%, $p = 0.012$) for 15 optimized beam directions.

Conclusions: For prostate cancer patients with metal hip implants, iCycle was able to automatically generate high quality, patient-specific IMRT plans with optimized coplanar or non-coplanar beam arrangements. Excluding only beamlets that would deliver dose to the PTV after passing through a prosthesis significantly improved OAR sparing for patients with bilateral implants as opposed to the AAPM taskgroup 63 recommendation. Non-coplanar beam arrangements and, to a larger extent, increasing the number of optimized treatment beams further improved plan quality.



PD-0493

Extreme hypofractionation in SBRT should be pursued with caution - impact of tumour reoxygenation

E. Lindblom¹, A. Dasu², I. Toma-Dasu³

¹Stockholm University, Medical Radiation Physics, Stockholm, Sweden

²County Council of Östergötland, Department of Radiation Physics UHL, Linköping, Sweden

³Stockholm University and Karolinska Institutet, Medical Radiation Physics, Stockholm, Sweden

Purpose/Objective: Stereotactic body radiotherapy (SBRT) for non-small-cell lung cancer (NSCLC) has led to promising local control and overall survival for fractionation schemes with increasingly high fractional doses. A point has however been reached where too few fractions may be used to allow efficient inter-fraction reoxygenation (IFR) of the hypoxic cells possibly residing in the tumours. It was the purpose of this study to investigate the impact of hypoxia and extreme hypofractionation on the tumour control probability (TCP) using realistic 3D-models of tumour oxygenation.

Materials and Methods: 3D-models of tumour oxygenation have been based on previous calculations of tumour oxygenation at cellular level for various distributions of intervascular distances. The models took into account dynamic changes in the oxygenation of the tumours between fractions. Simulations were performed for currently used fractionation schemes for NSCLC and for theoretical dose prescriptions that may be used in SBRT. Clinically relevant dose distributions were used to ensure the fulfilment of prescription details for dose escalation, dose to the PTV periphery and maximum dose. Cellular response was assessed with the LQ model at voxel level and a Poisson TCP model at tumour level.

Results: Calculated tumour control probabilities with IFR agree best with reported clinical local control for multi-fraction schemes (Table 1). The largest disagreement between the clinical figures and the

calculated values are seen for the single-fraction schemes which could be caused by other biophysical processes believed to take place at high doses, but not included in the model, such as vascular endothelial apoptosis. TCP curves for 1, 3 and 5 fractions with and without IFR (Figure 1) demonstrate the importance of allowing for IFR. Furthermore, they suggest that 3 or 5 fractions are enough to ensure IFR.

Table 1. Examples of calculated TCP with and without IFR for the dose schemes pertinent to current clinical practice in the SBRT treatment of NSCLC with clinical figures of survival and local control. Normal- and tumour tissue BED:s are also given.

† Dose range 24-40 Gy, 69% was given 37.5Gy

‡ Based on 60 Gy totaldoses given in 3, 5 and 8 fractions: 3x20 Gy(33%), 5x12 Gy (50%), 8x7.5 Gy(17%)

Dose prescr.	BED ₃ (Gy ₃)	BED ₁₀ (Gy ₁₀)	Treatment outcome		TCP (%)	
			Overall survival	Local control	No reox	IFR
3x12.5 Gy, 60% isodose	193.8	84.4	80% at 1 year† 75% at 2 years†	100% at 1 year† 87% at 2 years†	10	99
5x10 Gy, 80% isodose	216.7	100.0	90/63% at 3 years (Stage 1A/1B)	93/96% at 3 years (Stage 1A/1B)	0	99
8x7.5 Gy, 80% isodose	210.0	105.0	85.7% at 1 year† 54% at 2 years† 45.1% at 3 years†	89% at 2 years†	0	100

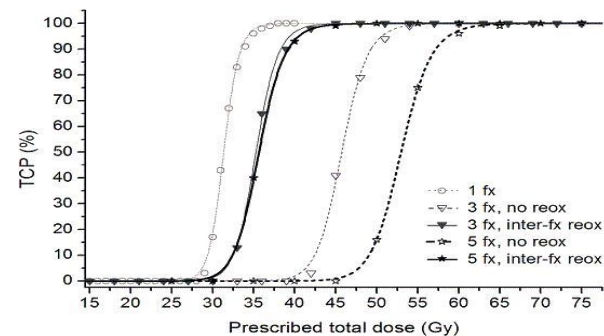


Figure 1. TCP curves obtained for 1 fx of 5-40 Gy per fx, and 3 and 5 fx of 5-25 Gy per fx, with and without IFR. Doses prescribed to the PTV-encompassing 69% isodose line.

Conclusions: Single-fraction stereotactic treatments may require a considerable increase in dose per fraction, well above fractional doses used today, to counteract the radioresistance of hypoxic cells. Although attractive from an economical and practical viewpoint, extreme hypofractionation in SBRT should therefore be pursued with caution as the reduced possibility for IFR may result in impaired local control.

PD-0494

NTCP for predicting mucosal toxicity in head-and-neck cancer patients after altered radiotherapy schedules.

L. Strigari¹, M. D'Andrea¹, P. Pinnarò², L. Marucci², C. Giordano², M. Benassi²

¹Regina Elena Cancer Institute, Lab. of Medical Physics and Expert Systems, Roma, Italy

²Regina Elena Cancer Institute, Radiotherapy Dept., Roma, Italy

Purpose/Objective: One of the worst radiation induced acute effects in treating head-and-neck (HN) cancer is grade 3 or higher acute (oral and pharyngeal) mucosal toxicity (AMT), caused by the killing/depletion of mucosa cells. Late toxicity are reported after altered radiotherapy schedules. The paper aims at testing a predictive model of the AMT, as well as late toxicity, in HN cancer patients receiving different radiotherapy schedules.

Materials and Methods: Various radio-therapeutic schedules have been reviewed and classified as tolerable or intolerable based on AMT

severity. A modified normal tissue complication probability (NTCP) model has been investigated to describe AMT data in radiotherapy regimes, both conventional and altered in dose and overall treatment time (OTT). We tested the hypothesis that such a model can also be applied to identify intolerable treatment and predict AMT and late toxicity. NTCP model has been compared with other published predictive models to identify schedules that are either tolerable or not. The Area Under Curve (AUC) was calculated for all models assuming treatment tolerance as the gold standard. NTCP model for late effect was also calculated. The correlation between AMT/late toxicity and the predicted toxicity rate was assessed by a Pearson correlation test.

Results: The AMT NTCP model was able to distinguish between acceptable and intolerable schedules among the data available for the study (AUC=0.84, 95%CI:0.75-0.92). In the equivalent dose at 2Gy/fraction (EQD2) versus OTT space, the proposed model shows a similar trend to that of models proposed by other Authors, but was superior in detecting some intolerable schedules. Moreover, it was able to predict the incidence of \geq G3 AMT. A correlation between the modified late NTCP model and \geq G3 late toxicity has been found as trend ($p=0.07$).

Conclusions: The proposed acute NTCP model is able to predict \geq G3 AMT after HN cancer radiotherapy and could be useful for designing altered/hypofractionated schedules in order to reduce the incidence of AMT. Late NTCP model was able to predict late toxicity but requires further improvements to increase the predictive power.

PD-0495

Prediction of rectal bleeding in prostate cancer radiotherapy: blind source separation approaches

A. Fargeas¹, L. Albera¹, A. Kachenoura¹, O. Acosta¹, G. Dréan¹, A. Simon¹, R. De Crevoisier²

¹INSERM U1099, Laboratoire du Traitement du Signal et de l'Image, Rennes, France

²Centre Eugène Marquis, Département de Radiothérapie, Rennes, France

Purpose/Objective: Current models for toxicity prediction in prostate cancer radiotherapy are based on the dose-volume histograms which lack of spatial accuracy. The goal is to propose new methods able to predict late rectal bleeding following high-dose prostate cancer radiotherapy. The aim is to fully exploit the tri-dimensional planned Dose Distribution (pDD) to study the correlation with rectal toxicity.

Materials and Methods: A total of 63 patients having received a dose of 80Gy in the prostate by IMRT have been included in the study. Twelve of them presented rectal bleeding (\geq grade 1) at two years. Only the 3D pDD within the rectum was analysed.

Our work has been divided in different steps:

1. Registration

Individuals' Computed Tomography (CT) from the planning and pDD were elastically registered using the demons algorithm to a single coordinate system by combining the CTs and organs delineations.

2. Training step

The training step consisted in learning from the data two vector subspaces spanning the 3D pDD of patients with toxicity and those of patients without toxicity, respectively. The different methods used to compute this subspaces have different constraints: orthogonality for Principal Component Analysis (PCA), mutual statistical independence for Independent Component Analysis (ICA).

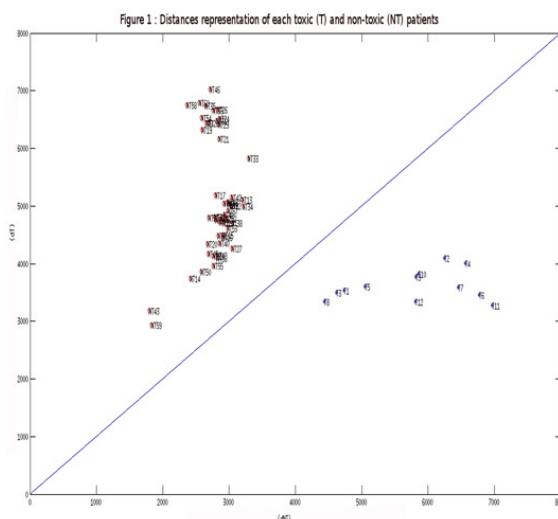
3. Validation

A new patient was classified by evaluating its distances to this two subspaces. We computed the euclidean distance between this patient and its orthogonal projector in the two subspaces. Eventually, this patient is classified as toxic if the distance (dt) from the subspace representing toxic patients is less than the distance from the other subspace (dnt).

4. Classification

A leave-one-out cross validation and statistical measures - sensitivity and specificity - were used to evaluate the classification performance. The sensitivity assesses the percentage of toxic patients who are correctly identified as having toxicity. The specificity assesses the percentage of patients who are correctly identified as not having toxicity.

Results: PCA method classified with 1 sensitivity and 0.76 specificity. ICA method allowed to classify perfectly rectal bleeding. Figure 1 shows the distance representation of each patient for ICA method. Two significant clusters were identified.



Conclusions: Our statistical approaches conjointly exploit 3D spatial patterns of dose, pDD and late rectal bleeding appear to be correlated. However, larger data base of patients will enable to use more robust classifiers. Our results will be compared with those obtained with existing models (i.e. NTCP).

PD-0496

Multi-centric learning with a federated IT infrastructure: application to 2-year lung-cancer survival prediction

A. Dekker¹, G. Nalbantov¹, C. Oberije¹, W. Wiessler², M. Eble³, W. Dries⁴, L. Janvary⁵, P. Bulens⁶, B. Krishnapuram², P. Lambin¹

¹GROW School for Oncology and Developmental Biology, Radiation Oncology (MAASTRO), Maastricht, The Netherlands

²Siemens, Medical Solutions, Malvern, USA

³University Hospital Aachen, Radiotherapy, Aachen, Germany

⁴Catharina Hospital, Radiotherapy, Eindhoven, The Netherlands

⁵CHU Liege, Radiotherapy, Liege, Belgium

⁶Limburg Oncologisch Centrum, Radiotherapy, Hasselt, Belgium

Purpose/Objective: To validate the hypothesis that multi-centric learning produces better models than models built on data from individual centers only.

Materials and Methods: We created an IT multi-centric network, which connects the databases of 5 clinical centers across 3 European countries. The network is a federated database where certain rules apply to ensure that data privacy is preserved, data never leaves the boundaries of its institution of origin, and secure traffic through firewalls is achieved. We then tested whether learning from federated data via the network gives advantage over single-center learning in the following way. A dataset 322 non-operable and non-metastatic non-small cell lung cancer patients treated with definite (chemo)radiotherapy was distributed with unequal proportions across 5 centers. A model was built for each center using only the locally available data. A distributed learning model was deployed in the IT network which has a read-only, no-copy access to local data. The chosen model was the Support Vector Machines (SVM) classifier, solved with the Alternating Direction Method of Multipliers method, which enables learning from data stored in different locations in a distributed way. The biggest advantage of this method is that the model learnt from scattered data across centers is exactly the same as if the data was centrally available.

Results: The 5 centers had the following number of lung cancer patients available in the infrastructure: 186, 52, 45, 7 and 32, respectively. The predicted variable was 2-year survival, with predictor variables gender, World Health Organization performance status, forced expiratory volume in 1 second, number of positive lymph node stations, gross tumor volume and biologically-equivalent (at 2 Gray) total dose. No survival data was censored. We used the data at center 1 as an external validation set within the network. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC). Models built separately on centers 2 to 5 had AUC's of 0.75, 0.68, 0.61 and 0.72 when validated on center 1. The AUC values fluctuate substantially, which reflects to a high degree the current model-learning reality and leaves open the question of how a combined-data model would perform. We can answer this question using the network: the distributed SVM model built on all data from centers 2 to 5 without any data leaving its origin had an AUC of 0.77 on center 1 (see Figure 1).